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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/560,372	04/28/2000	Alan R. Tall	61766/JPW/GJG	3550

7590 08/28/2003

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EXAMINER

PARAS JR, PETER

ART UNIT

PAPER NUMBER

1632

18

DATE MAILED: 08/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/560,372

Applicant(s)

TALL, ALAN R.

Examiner

Peter Paras, Jr.

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1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 April 2003 and 23 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,5-16,18-25,50 and 51 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,5-16,18-25,50 and 51 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

Applicant's amendment received on 4/21/03 has been entered. Claims 3-4 have been cancelled. Claims 1 and 49 have been amended.

Applicant's supplemental amendment received on 6/23/03 has been entered. Claims 1, 10, 16 and 50 have been amended. Claim 49 has been cancelled. Claims 1-2, 5-16, 18-25, and 50-51 are pending and are under current consideration.

### ***Specification***

The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112, 1<sup>st</sup> paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of expressing foreign DNA in a host cell *in vitro*, does not reasonably provide enablement for a method of expressing foreign DNA in a host cell *in vivo*. The specification does not enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The aspects of the previous enablement rejection directed to methods of transforming a host cell *in vivo* are maintained for the reasons of record advanced on pages 4-6 of the Office action mailed on 1/16/03. Aspects of the previous enablement rejection directed to variants of the promoter sequence of the invention have been withdrawn.

Applicant's arguments filed on 4/21/03 have been fully considered but are not found persuasive. Applicants have argued that introduction and expression of recombinant expression constructs in living cells has been known to those skilled in the art for twenty years. Applicants further argue that many techniques have been developed for introducing foreign DNA into mammalian cells. Applicants submit that the claims are enabled to the extent of reading on transformation of living cells. See page 9 of the amendment received on 4/21/03.

In response, the Examiner maintains that methods of transforming cells *in vivo* are encompassed within the art of gene therapy. When taken with the teachings of the specification the claims are properly interpreted to embrace gene therapy. See for example pages 5 and 13-15. The Examiner further maintains that the art of gene therapy was unpredictable at the time the claimed invention was made and has remained unpredictable thereafter. The instant specification has failed to provide adequate guidance that would allow the skilled artisan to transform and express a foreign DNA sequence in a host cell *in vivo*. Furthermore, the instant specification has not provided a correlation between expression of a foreign gene in a cell *in vivo* and any

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therapeutic benefit. Moreover, the instant specification has not provided adequate guidance that overcomes issues of unpredictability, within the field of gene therapy, relating to cell targeting, mode of administration of an expression construct, level of expression of a heterologous nucleotide sequence necessary to provide therapeutic benefit, and the fate of the expressed heterologous protein *in vivo*. Verma and Anderson (see page 6 of the Office action mailed on 1/16/03) support the unpredictability of gene therapy. Although methods for introducing a construct into a living cell are known, this argument appears to offpoint in light of the issues of unpredictability relating to gene therapy. Given the teachings of the specification it does not appear that there are any uses for the claimed methods other than for providing therapy. Amending the claims to read on an a method for expressing a foreign DNA in a host cell *in vitro* would be sufficient to overcome the instant rejection.

Accordingly, the rejection is maintained for the reasons of record.

The previous rejection of claims 1, 3-15, 18-25, and 49 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention has been withdrawn.

***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 5-16, 18-25 and 50-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite as written. The claim is directed to a promoter comprising the nucleotide sequence beginning at bp -469 and ending at bp +101 of the nucleotide sequence set forth in SEQ ID NO: 1 and to a promoter comprising the nucleotide sequence beginning at bp -101 and ending at bp -32 of the nucleotide sequence set forth in SEQ ID NO: 1. The claim is indefinite because the nucleotide sequence set forth in SEQ ID NO: 1 does not comprise nucleotides that have negative numbering. As such it is not clear which nucleotide bases of SEQ ID NO: 1 correlate to the sequence beginning at bp -469 and ending at bp +101 or to the sequence beginning at bp -101 and ending at bp -32. Neither the specification nor the claim has provided a numbering system that provides a correlation between the claimed sequences and SEQ ID NO: 1. Figure 3, as described on page 7, provides the nucleotide sequence set forth in SEQ ID NO: 1 in the context of an actual promoter sequence by depicting the regions of SEQ ID NO: 1 that are upstream and downstream of the transcription initiation site. For example the 5' end of the sequence is position -928 and the 3' end of the sequence is +101. A Sac1 restriction site is positioned at -469. Comparison of the sequences of Figure 3 and SEQ ID NO: 1 suggests that a discrepancy exists with respect to position -

469 (the Sac1 site). It appears that the Sac1 site as shown in Figure 3 is not at position -469 but rather is at position -471. Also, it appears that the length of the 5' end of exon 1 as shown by the bolded sequence in figure 3 is longer than 101 bases suggesting that the sequence does not end at position +101 as discussed in the specification on pages 7-8. In light of the above, the Examiner suggests amending the claims to recite a correlation between the exact sequences in Figure 3 and SEQ ID NO: 1 as embraced by the claim in steps b and c. Applicants are encouraged to check for additional discrepancies that may be related to step c of the claim. Claims 2, 5-16, 18-25 and 50-51 depend from claim 1.

### **Conclusion**

**No claim is allowed.**

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Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (703) 305-3388.

Peter Paras, Jr.

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**PETER PARAS**  
**PATENT EXAMINER**

